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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR		ATTORNEY DOCKET NO.
09/099,823	06/19/98	BILLING-MEDEL	P	0200-0023.20

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EXAMINER	
GOLDBERG, J	
ART UNIT	**PAPER NUMBER**
1655	16

DATE MAILED: 09/14/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	09/099,823	BILLING-MEDEL ET AL.	
	Examiner	Art Unit	
	Jeanine A Enewold Goldberg	1655	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

1)☒ Responsive to communication(s) filed on *21 August 2000* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-49* is/are pending in the application.

4a) Of the above claim(s) *17-29,31,32,34,36,37,43 and 44* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-16,30,33,35,38-42 and 45-49* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a)☐ All b)☐ Some * c)☐ None of the CERTIFIED copies of the priority documents have been:

1.☐ received.

2.☐ received in Application No. (Series Code / Serial Number) _____ .

3.☐ received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. & 119(e).

Attachment(s)

15) ☐ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other: .

DETAILED ACTION

1. This action is in response to the papers filed August 21, 2000. Currently, claims 1-49 are pending. Claims 17-29, 31-32, 34, 36-37, 43-44 have been withdrawn from consideration. All arguments have been thoroughly reviewed but are deemed non-persuasive for the reasons which follow. This action is made FINAL.

2. Any objections and rejections not reiterated below are hereby withdrawn.

Priority

3. Although, this application is a continuation-in-part of the parent application 08/879,354, additional materials (SEQ ID NO: 3, SEQ ID NO: 4 and SEQ ID NO: 5) are added to all of the elected claims in this application. Therefore, the claims considered receive priority back to the instant filing date of June 19, 1998 rather than to the effective filing date of the parent application 08/879,354 of June 1997.

Response to Arguments

The response asserts SEQ ID NO: 3 is new, except for the last four nucleotides, which is not representative of SEQ ID NO: 3 of the instant application. The response asserts that positions 1-357 of SEQ ID NO: 4 and SEQ ID 5 are the same as SEQ ID NO: 3 of the parent. It is now unclear how these regions are different such that they are claimed twice in a single claim. Additionally, it is noted that 08/879,354, filed June 20, 1997, does not disclose any amino acid sequences of 170 amino acids, thus, SEQ ID NO: 22, is not disclosed.

New Matter

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1, 3, 6, 10-11, 15, 30, 33, 38-40, 45-49 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In the amended claims, reference to "lipocalin-encoding" are included. The amendment proposes that the new limitations was known to one skilled in the art. However, the specification does not describe or discuses "lipocalin-encoding". Instead the specification describes BS124 nucleotide sequences SEQ ID NO: 1-5. This description does not support lipocalin-encoding. While the response submits an article filed after the filing date as support for the added amendment, the further characterization of the "BS124" polynucleotides after the filing date may not be entered into the specification. The specification provided no characterization for the BS124 polynucleotides nor any homology study which showed a relationship to this family of lipocalins at the time of filing. The concept of "lipocalin-encoding polynucleotides" does not appear to be part of the originally filed disclosure. Therefore, "lipocalin-encoding" constitutes new matter.

Applicant is required to cancel the new matter in the reply to this Office Action.

Maintained Rejections

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1-16, 30, 33, 35, 38-42 and newly added claims 45-49 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for detecting the presence of a target BS124 polynucleotide comprising SEQ ID NO: 1-5 and the complements of SEQ ID NO: 1-5, does not reasonably provide enablement for BS124 polynucleotides having "at least 50% identity with" SEQ ID NO: 1-5 and fragments or complements thereof, or for genes encoding BS124 proteins having "at least 50% identity" with SEQ ID NO: 22. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

It is well established that to claim a chemical compound, such as a polynucleotide, the inventor must be able to define the compound so as to distinguish the compound from other materials. The claimed compound must be defined in terms so as to provide a permanent and definite idea of the complete and operative invention. In the instant case, the claimed polynucleotides have not been clearly defined in terms

of structure and/or function, and therefore one cannot make and use the polynucleotides as claimed. As stated in Vaek (CAFC 20 USPQ2d 1438, the "specification must teach those of skill in the art how to make and use the invention as broadly as it is claimed." However, in order to be able to make an invention, one must be able to clearly define that invention.

The claims are drawn to a method of detecting a polynucleotide having "at least 50% identity with" SEQ ID NO:s 1-5 and fragments and complements thereof (Claims 1-9), to polynucleotides having "at least 50% identity with" SEQ ID NO:s 1-5, and fragments and complements thereof, and to a gene which codes for an BS124 protein "which comprises an amino acid sequence having at least 50% identity to SEQ ID NO: 22" (Claim 38). The specification teaches a single BS124 consensus polynucleotide, SEQ ID NO: 5, the sequence of which was assembled from 3 EST clones (SEQ ID NO:1-3) and the fill-length clone (SEQ ID NO: 4) (pg. 57).

Applicant's specification discloses a single BS124 gene sequence and a single BS124 protein sequence. Yet Applicant's claims, which are to sequences having "at least 50% identity" with a few sequences taught in the specification, may encompass thousands of polynucleotides. As discussed below, Applicant's definition of "% identity" is insufficient to provide a skilled artisan with the guidance necessary to clearly define the sequences encompassed by this claim language. Without specific teachings with respect to the methods used to determine "% identity", a skilled artisan could not be expected to identify or make the polynucleotides encompassed by the instant claims. Furthermore, irrespective of how "% identity" is defined, it is clear that by any definition

of "% identity", may sequences encompassed by applicant's claims, and particularly those having "at least 50% identity" with fragments of the sequences taught in the specification, would bear little resemblance to the single BS124 consensus sequence that Applicant has taught. Neither the specification nor the claims set forth any particular structural or functional characteristics that a skilled artisan could use to identify polynucleotides that constitute BS124 polynucleotides, other than those described by SEQ ID NO. The term "BS124" is not an art recognized term, and thus the prior art is silent with respect to structural and functional features that may be used to identify such polynucleotides. Furthermore, in teaching a single BS124 polynucleotide sequence and a single BS124 protein sequence, applicant clearly has not taught the isolation of a representative number of polynucleotides that fall within the scope of the large genus encompassed by the instant claims. Thus, while the teachings of the specification and of the prior art would enable a skilled artisan to make and used polynucleotides comprising SEQ ID NO: 1-5 and the complements of SEQ ID NO: 1-5, as well as polynucleotides encoding SEQ ID NO: 22, it is unpredictable as to whether a skilled artisan could make and use BS124 polynucleotides having "at least 50% identity" with SEQ ID NO: 1-5 and fragments and complements thereof, or genes encoding BS124 proteins having "at least 50% identity" with SEQ ID NO: 22. It would require undue experimentation for a skilled artisan to make and use the invention as broadly as it is claimed.

Response to Arguments

The response traverses the rejection. The response asserts that the percent identity has been amended to recite "over the entire length" of the SEQ ID NO:s. However, This argument has been reviewed but is not convincing because the claims remain drawn to polynucleotides which were not described such that the skilled artisan could make and use the polynucleotides. Neither the specification nor the claims set forth any particular structural or functional characteristics that a skilled artisan could use to identify polynucleotides that constitute BS124 polynucleotides, other than those described by SEQ ID NO." Thus sequences with only 90% identity with SEQUENCE ID NO: 1, 2, 3, or position 1-357 of SEQ ID NO: 4, or position 1-357 of SEQ ID NO: 5 would have little resemblance to a breast-specific polynucleotide of the claimed invention. Specifically, it would be expected that methods for detecting breast-specific nucleotides with such sequences which are 90% identical to SEQ ID NO: 1, 2, 3, or 90% identical to positions 1-357 of SEQ ID NO: 4, 5, would detect polynucleotides which were not breast-specific and which would have little to no correlation to the presence of breast disease. Thus, it would still require undue experimentation for the skilled artisan to practice the instant claims as broadly as claimed.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1-16, 30, 33, 35, 38-42 and newly added claims 45-49 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The essential limitations of the claims are drawn to polynucleotides having 50% identity with SEQ ID NO: 1, 2 or having 60% identity with SEQ ID NO: 4, 5. Moreover, the claims are drawn to correlating the detection of these polynucleotides to breast tissue disease.

The specification teaches the polynucleotides consisting of SEQ ID NO: 1-5. The specification teaches a single BS124 consensus polynucleotide, SEQ ID NO: 5, the sequence of which was assembled from 3 EST clones (SEQ ID NO:1-3) and the fill-length clone (SEQ ID NO: 4) (pg. 57). The specification only analyzed breast cancer tissue in the specification.

There is not adequate description of the genus of polynucleotides having 50% identity with SEQ ID NO: 1, 2 or having 60% identity with SEQ ID NO: 4, 5. The specification only discloses polynucleotides consisting of SEQ ID NO: 1, 2, 4 and 5 within the scope of the genus: having 50% identity with SEQ ID NO: 1, 2 or having 60% identity with SEQ ID NO: 4, 5. Yet Applicant's claims, which are to sequences having "at least 50% identity" with a few sequences taught in the specification, may encompass thousands of polynucleotides. The general knowledge in the art concerning having 50% identity with SEQ ID NO: 1, 2 or having 60% identity with SEQ ID NO: 4, 5 does not

provide any indication of how to readily identify these polynucleotides. There is substantial variability among the species of nucleic acids encompassed in the scope of the claim. The specification has also not defined a structural feature of the polynucleotides having 50% or 60% identity which would be common to all members of the genus that constitutes a substantial portion of the genus. Neither the specification nor the claims set forth any particular structural or functional characteristics that a skilled artisan could use to identify polynucleotides that constitute BS124 polynucleotides, other than those described by SEQ ID NO. The specification provides no guidance in the specification with respect to structural and functional features that may be used to identify such polynucleotides.

Additionally, "breast tissue disease" is a broad term, which is not limited to breast cancer but would also encompass any type of disease of breast tissue, including infections of breast tissue, and mammary gland disorders, for example. The only breast disease tissue analyzed in the specification was breast cancer tissue.

Furthermore, in teaching a single BS124 polynucleotide sequence and a single BS124 protein sequence, applicant clearly has not taught the isolation of a representative number of polynucleotides that fall within the scope of the large genus encompassed by the instant claims. Thus one of skill in the art would conclude that applicant was not in possession of the claimed "polynucleotides having 50% identity with SEQ ID NO: 1, 2 or having 60% identity with SEQ ID NO: 4, 5" because the description of only polynucleotides consisting of SEQ ID NO: 1, 2, 3, 4, and 5 of this genus is not representative of the polynucleotides of the genus and is insufficient to

support the claims. Thus, the specification does not adequately provide a written description for polynucleotides having 50% identity with SEQ ID NO: 1, 2 or having 60% identity with SEQ ID NO: 4, 5.

Response to Arguments

The response traverses the rejection. The response asserts that the raised percent identity and amending the claims to specify that the claimed nucleic acid sequences encode a lipocalin protein. This argument has been reviewed but is not convincing because the claims while amended to recite a higher percent identity, remains drawn to nucleic acids which have not been described. Those nucleic acids which are 90% identity with SEQ ID NO: 1-3 or 90% identity with SEQ ID NO: 4 or 5 positions 1-357. The specification does not teach the broadly claimed sequences having 90% identity or a representative number of the claimed sequences. Thus for the reasons above and those already of record, the rejection is maintained.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Newly added claim 49 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for detecting SEQ ID NO: 1, 2, 4, 5, does not reasonably provide enablement for detecting a polynucleotide indicative of breast tissue disease by detecting a sequence having at least 50% identity with SEQ ID NO: 1, 2, or

at least 60% identity with SEQ ID NO: 4, 5. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to the invention commensurate in scope with these claims.

The claims are broadly drawn to a method for detecting a diagnostic polynucleotide nor a polynucleotide indicative of breast tissue disease by detecting a sequence having at least 50% identity with SEQ ID NO: 1, 2, or at least 60% identity with SEQ ID NO: 4, 5.

The specification teaches BS124 was found in 5.9% of breast tissue libraries and only in .3% of non-breast libraries (pg. 57, lines 21-24). Further, the specification teaches that BS124 RNA was isolated from both breast tissues and from non-breast tissues (pg. 59). The specification teaches that through a Northern blot analysis the BS124 probe detected RNA in the breast sample and the testis sample, but not in any of the other non-lung RNA samples (pg. 65, lines 27-30). The BS124 probe detected RNA in 2/6 breast cancer specimens but not in any of the five normal breast samples (pg. 66, lines 1-5).

Additionally, "breast tissue disease" is a broad term, which is not limited to breast cancer but would also encompass any type of disease of breast tissue, including infections of breast tissue, and mammary gland disorders, for example. The only breast disease tissue analyzed in the specification was breast cancer tissue.

Correlating the presence of SEQ ID NO: 1, 2, 4, 5 to the presence of breast tissue disease in a patient would be unpredictable since the specification teaches that BS124 was detected in both breast tissue and testis tissue. It would be undue

experimentation for the ordinary artisan to perform the additional studies needed to determine whether the detection of the polynucleotide in testis tissue is in fact indicative of breast tissue disease. It would be unpredictable to detect any breast tissue disease with BS124 since no guide was provided in the specification to any breast tissue diseases other than breast cancer. The wide variety of different disease encompassed by the broad term breast tissue disease have no pathological or metabolic relationship to cancer.

Response to Arguments

The response traverses the rejection. The response asserts that the claims are limited to "breast cancer". This argument has been reviewed but is not convincing because Claim 49 is drawn to breast cancer disease. Thus for the reasons above and those already of record, the rejection is maintained.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

8. Claim 38 is rejected under 35 U.S.C. 102(e) as being clearly anticipated by Conklin (US Pat 6,020,163, February 2000).

Conklin teaches a lipocalin homolog polypeptide, SEQ ID NO: 2, which contains 170 amino acids which are 100% identical to the 170 amino acids of SEQ ID NO: 22. Further, Conklin teaches that SEQ ID NO: 5 is a polynucleotide which encodes the amino acid of SEQ ID NO: 2. Thus the claimed invention is anticipated by the teachings of Conklin.

Response to Arguments

The response traverses the rejection. The response asserts that Conklin has a provisional priority date of August 6, 1997, however, the instant case has a priority date of June 20, 1997. This argument has been reviewed but is not convincing because SEQ ID NO: 22 was not disclosed prior to June 19, 1998, the instant filing date. Thus, Conklin properly is a 102(e) reference. Thus for the reasons above and those already of record, the rejection is maintained.

Conclusion

9. No claims allowable.

10. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jeanine Enewold whose telephone number is (703) 306-5817. The examiner can normally be reached Monday-Thursday from 7:00 AM to 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (703) 308-1152. The fax number for this Group is (703) 305- 3014.

Any inquiry of a general nature should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Jeanine Enewold Goldberg
September 12, 2000

LISA B. ARTHUR
PRIMARY EXAMINER
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